REMARKS

Claims 2-15 are canceled. New claims 16-33 are added. Claims 1 and 16-33 are pending.

Support for Amendments

The specification is amended to replace the chemical structure for formula 2 with the chemical name. Applicants believe the chemical name provides a more precise designation of the correct stereochemistry of Applicants' preferred embodiment. Therefore, the specification is amended to replace the chemical structure for formula 2 with the chemical name: (4S)-MeHex-D-Val-L-Thr-L-Val-D-Val-D-Pro-L-Orn-D-*allo*-Ile-*cyclo*(D-*allo*-Thr-D-*allo*-Ile-D-Val-L-Phe-*Z*-Dhb-L-Val). Support for the name can be found on page 17, lines 19-20, where the chemical name is given and equated with (4S)methylhexanoic KF. The compound is part of Example 1, which provides a synthesis for the named compound. The positions of the amino acids, including the L or D designation, are provided in Table 1 where, for example, it is specified that Val 1 (the valine next to Z-Dhb) has the L designation. See pages 18-19. See also page 16 of the specification, which refers to WO 01/58934, which points out that where L or D is not designated, it is commonly understood that the default amino acid is L.

Claims 16-17 are supported by previously presented claim 1.

Claims 18-20 are supported by previously presented claim 2, and page 17, lines 19-20, where the chemical name is given, and in Example 1, which provides a synthesis for the named compound.

Claim 21 is supported by previously presented claim 3.

Claim 22 is supported by previously presented claim 10.

Claims 23-25 are supported by previously presented claims 11-13.

Claims 26-31 are supported by previously presented claims 4-7 and 14-15 and Examples 3 and 8.

Claims 32-33 are supported by previously presented claims 8-9.

No new matter is added.

Information Disclosure Statement

Applicants submit herewith an Information Disclosure Statement (IDS) and request consideration of the IDS by the examiner.

Election of Species

The Office Action indicates that the claims are directed to distinct species of the claimed invention for claims 4-7, 9, and 14-15 as far as specific type of cancer (e.g. breast cancer), viral infection (claim 9) or fungal infection (claim 9). The Office Action also indicates that claims 1 and 29 are generic (Applicants note that only claims 1-15 were pending at the time of the Office Action). The Office Action indicates that a provisional election was made without traverse to prosecute the species "breast cancer", and that affirmation of this election must be made by Applicant in replying to the Office Action. The Office Action states that the "claims are only withdrawn as to non-elected compound (e.g. other forms of cancer) from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention" (Office Action, page 3, lines 15-17).

Applicants confirm the election of the species "breast cancer," without traverse during a telephonic election of species as indicated in the Office Action. However, in view of the

examination of the full scope of the claims in the Office Action, Applicants understand that the application will continue to be examined for the entire scope of the claims.

Double Patenting

Claims 1-15 are provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-4 and 6-47 of copending application 10/492,670 (published as US 2005/0054555). Applicants respectfully traverse the rejection. However, since the rejection is provisional and US 10/492,670 is awaiting examination, Applicants respectfully request that the rejection be held in abeyance pending the determination of patentable subject matter. Applicants suggest that if all other rejections are overcome, it is appropriate to withdraw the provisional double-patenting rejection and allow the instant application to issue, and apply any double-patenting rejections deemed necessary by the Examiner to the later application, as directed by the MPEP:

> If the "provisional" double patenting rejection is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

See MPEP 804.1B. Applicants reserve their right to provide arguments against the rejection at a later time.

Rejections Under 35 U.S.C. § 112, 1st paragraph (scope of enablement)

Claims 1-15 are rejected under 35 U.S.C. § 112, 1st paragraph for lack of enablement for the entire scope of the claims. The Office Action states that the specification "while being enabling for pharmaceutically acceptable salts of kahalalide F "4-methylhexyl",

does not reasonably provide enablement for any prodrug, tautomer, or solvate thereof" (see Office Action, paragraph bridging pages 4-5).

Applicants thank the examiner for the indication that the claims are enabling for the compounds and their pharmaceutically acceptable salts. As amended, claims 16 and 19 are directed to compounds and pharmaceutically acceptable salts thereof. Therefore, Applicants respectfully request that the rejection be withdrawn for claims 16 and 19 and dependent claims to the extent that the claims depend from claims 16 and 19.

With respect to independent claim 1 and its dependent claims which can include prodrugs, tautomers, or solvates (i.e. claims 1, 17-18, and 20-33), Applicants respectfully traverse the rejection for lack of enablement for prodrugs, tautomers, or solvates.

Applicants note that the cited passages from the Vippagunta reference relied upon by the Office Action are silent with respect to tautomers, and no discussion specific to tautomers is included in the Office Action's analysis of the factors contributing to enablement (or lack thereof). Therefore, the Office Action has failed to show how tautomers lack enablement. Furthermore, tautomers are well known in the field of organic chemistry. A review of any standard undergraduate organic chemistry textbook will show that tautomers "are structural isomers that are formally related only by the shift of a hydrogen and one or more π-bonds" (see Loudon, (Organic Chemistry, 2nd Edition, 1988, The Benjamin/Cummings Publishing Company, Inc., page 924)). For the convenience of the examiner, Applicants attach 3 pages from Loudon as part of the Information Disclosure Statement, which is an example of an undergraduate organic chemistry textbook that provides a definition for tautomers. The page shows that the concept and practice of determining tautomerization is a standard concept taught in undergraduate level organic chemistry. In fact, Loudon clearly shows that one can predict the tautomers of a given

structure (see problem 6 on page 926 of Loudon). Therefore, one of ordinary skill in the art would readily be able to determine which structures constitute tautomers of the claimed compounds.

Applicants note that the cited passages from the Vippagunta reference relied upon by the Office Action are also silent with respect to prodrugs, and no discussion specific to prodrugs is included in the Office Action's analysis of the factors contributing to enablement (or lack thereof). Therefore, the Office Action has failed to show how prodrugs lack enablement. Furthermore, the Office Action appears to be applying an inconsistent standard with respect to the term prodrug as compared to other applications. Prodrugs are well-known in the art, and routinely claimed and allowed in other patents. For example, see US Patent 7,067,257, which was recently examined and allowed by Examiner Audet. In view of the fact that prodrugs are known in the art and routinely allowed in other patents, Applicants assert that lack of enablement has not been shown.

With regard to solvates (also referred to as pseudopolymorphs by Vippagunta), the Office Action appears to be requiring an element that is not claimed. Specifically, the Office Action appears to be requiring that in order for solvates to be enabled, that it must be possible to predict from first principles each and every possible solvate that could be formed. However, the claims do not encompass a method of predicting which solvates can and cannot be formed.

Applicants traverse the requirement that such a level of prediction is necessary for enablement to a claim encompassing a solvate. Specifically, many aspects of the chemical arts are empirical in nature. As such, Vippagunta itself provides the practicing chemist with a concise summary of the techniques for confirming the presence of a solvate. For example, Vippagunta teaches that "Various analytical methods are being currently used to characterize the crystalline

form of the drug during the various steps of processing and development. These methods have been reviewed recently in detail by many authors" (Vippagunta, page 5, right column, lines 20-45). Techniques taught by Vippagunta for analyzing solvates include single-crystal X-ray diffractometry, FTIR, FT Raman spectroscopy, SSNMR, UV-Vis spectroscopy, fluorescence spectroscopy, differential scanning calorimetry, thermogravimetric analysis, and optical microscopy (i.e. visual observation). In fact, based on the state of the analytical techniques provided by Vippagunta, the process of confirming the presence of a solvate would appear to be straightforward (i.e. isolating the compound as a solid from a solvent, and then using the one of the readily-available techniques taught by Vippagunta to confirm the presence of a solvate). In addition, the number of solvents that one might choose to work with is in actuality limited by a number of factors such as commercial feasibility, compatibility with the claimed compound, or suitability for *in vivo* use. Therefore, the number of potential solvents to create solvates is not unlimited.

In summary, solvates as claimed are enabled because the current state of the art allows for routine empirical characterization of solvates without undue experimentation.

Claims 4-7, 9, and 14-15 are rejected under 35 U.S.C. § 112, 1st paragraph for lack of enablement for the entire scope of the claims. The Office Action states that the specification "while being enabling for treating cancer from hepatocellular carcinoma (Example 8), human live[r] adenocarcinoma (Example 8), breast cancer (Example 6), and prostate cancer (Example 7), using kahalalide F "4-methylhexyl" or pharmaceutically acceptable salts thereof; does not reasonably provide enablement for treating any cancer, or a viral or fungal infection"

(see Office Action, last paragraph, page 7). New claims 26-33 correspond to previously presented claims 4-7, 9, and 14-15.

Applicants thank the examiner for the indication that the claims are enabling for treating cancer from hepatocellular carcinoma, human liver adenocarcinoma, breast cancer, and prostate cancer. As amended, claim 31 includes language directed to cancer from hepatocellular carcinoma, human liver adenocarcinoma, breast cancer, and prostate cancer, which subject matter has been deemed enabled by the Office Action. Therefore, Applicants respectfully request that the rejection be withdrawn for claim 31.

Claim 30 includes language that the cancer is selected from prostate cancer, breast cancer, hepatocellular carcinoma, melanoma, colorectal cancer, renal cancer, ovarian cancer, lung cancer, epithelial cancer, pancreatic cancer, and tumors that overexpress the Her2/neu oncogene. Applicants direct the Examiner's attention to Example 3 for *in vitro* data of compounds according to the invention against a panel of cancer cell lines. Accordingly, data is provided against leukemia (K-562), lung cancer (A-549), melanoma (SK-MEL-28), colon cancer (HT-29, LoVo, LoVo-Dox), tumors that overexpress the Her2/neu oncogene (SK-BR-3), ovarian cancer (IGROV-1 and IGROV-ET), cervical cancer and/or epithelial cancer (HeLa and HeLa-APL), and pancreas cancer and/or epithelial cancer (Panc-1). Additionally, example 8 also provides activity data against melanoma (MEL-28) and pancreas (Panc-1) cancers in hollow fiber assays. The Office Action points to Example 8 as providing enablement for hepatocellular carcinoma and human liver adenocarcinoma. Applicants suggest that Example 8 also provides enablement for melanoma and pancreas cancers, and that Example 3 provides enablement for the remainder of the listed cancers. Therefore, Applicants respectfully request that the rejection be withdrawn for claim 30.

With respect to claims 26-29 and 32-33, Applicants respectfully traverse the rejection to the extent that it may be applied to the new claims. The Office Action relies on the Gura reference to support the Office Action position regarding the difficulty of identifying compounds that will succeed in human clinical trials. However, the Gura reference does not address the specific *in vitro* and *in vivo* tests in Examples 3 and 5-8 in the specification. In addition, the problem identified by Gura ("sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile" as quoted on page 8 of the Office Action) does not support the position of the Office Action, since the instant claims already identify the compound of formula 1 as the compound of interest. In addition, in describing the amount of guidance, the Office Action overlooks the broad scope of guidance provided in Example 3. Reliance on the Gura reference would appear to require that enablement for purposes of patent protection requires FDA-approved treatments. Enablement as required by 35 U.S.C. 112, first paragraph, is not the same standard as required by the FDA for evaluation of phase III human clinical trials, and such a requirement should not be imported into the patent statutes. Applicants believe that the guidance provided in Examples 3 and 5-8 provide sufficient enablement of the claims to their entire scope.

In view of the large amount of data provided by the specification, and the inappropriateness of the Gura reference, Applicants respectfully request that the rejection for lack of enablement be withdrawn as it may be applied to claims 26-29 and 32-33.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

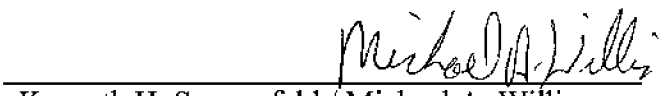
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. 13566.105012.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13566.105012.

Respectfully submitted,
King & Spalding, LLP

Dated: April 2, 2007

By: 

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